

A -- The present technology circumvents the limitations of the prior art and provides an entirely novel means for the screening of very large polypeptide libraries. In particular, the invention overcomes deficiencies in the prior art by providing a rapid approach for isolating proteins that bind to small molecules and peptides via "display-less" library screening. A description of an example of such a process in accordance with the invention is described for illustrative purposes in FIG. 1. In the technique, libraries of candidate binding proteins, such as antibody sequences, are expressed in soluble form in the periplasmic space of gram negative bacteria, such as *Escherichia coli*, and are mixed with a labeled ligand. The periplasm comprises the space defined by the inner and outer membranes of a gram-negative bacterium.

Please replace the paragraph at page 62, lines 14-28 with the following:

A -- This example summarizes the screening of a repertoire antibody library to the ligand TNB (trinitrobenzene). Library screening was initiated by first carrying out three rounds of phage panning of a repertoire library (Griffin -1 library) using standard protocols (see example 6, also described in www.mrc-cpe.cam.ac.uk/~phage/g1p.html). Phage rescued from various rounds of panning were used to infect the *E. coli* ABLE C. The cells were grown to mid-exponential phase, induced for expression of scFv antibodies as described above and labeled with 100 nM TNBS conjugated to the fluorescent dye Cy5. The labeled cells were analyzed by flow cytometry using a Cytomation MoFlo instrument equipped with a 5 mM diode laser emitting at 633 nm. Highly fluorescent clones were isolated on membrane filters and analyzed further. Three out of 10 clones isolated by FACS were analyzed further and found to exhibit strong binding to a TNBS-BSA conjugate. Sequence analysis confirmed that one of the TNBS specific clones had also been found by phage display. However, the two other clones isolated by the present invention (periplasmic expression of the library and FACS screening) did not correspond to any of the clones isolated by phage panning.

In the Claims:

Please amend claim 30 as indicated below:

A3 30. (Amended) The method of claim 1, wherein said selecting comprises fluorescent activated cell sorting.